UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 30 2000

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

The Honorable Thomas Bliley
Chair, House Committee on Commerce
U.S. House of Representatives
Washington, DC 20515-6115

Dear Chairman Bliley:

Thank you for your letter of August 9 to Administrator Browner concerning the Environmental Protection Agency's (EPA) Special Review of the pesticide atrazine. Because this office is responsible for regulating pesticides, Administrator Browner asked me to reply to your letter in which you ask for clarification of several issues that have arisen in recent meetings between Agency officials and staff of the House Committee on Commerce. Our response to your questions is enclosed.

Please let me assure you that I share your commitment to ensuring that Americans have the safest and most abundant food supply in the world. As the Agency responsible for implementing laws that affect the safety of our nation's food supply, we are dedicated to using the best science in our decisions concerning the use of pesticides. I hope that the enclosed information adequately addresses your concerns. If I may be of further service, please let me know.

Sincerely yours,

Susan H. Wayland
Acting Assistant Administrator

Enclosure

Questions from Chairman Bliley

1. On January 14, 1999, Marcia Mulkey, Director of EPA's Office of Pesticide Programs, provided a written commitment to the Wisconsin Agribusiness Council that EPA's draft cancer guidelines "must be finalized before we can definitively revise the cancer estimate for atrazine." At the Agency's meeting with the Committee staff on June 26, 2000, and in follow-up written communications to the Committee, the Agency appears to have reneged on that commitment, stating that "it is appropriate to begin considering the proposed guidelines even before they are officially completed . . . . [n]either the 1996 nor the 1999 versions of the draft guidelines are at odds with the 1986 guidelines, but are an expansion."

a. Please describe the status of the Agency's efforts to finalize the draft cancer assessment guidelines. Why has the Agency not finalized the guidelines to date? Specifically identify each area in which the Agency believes the 1996 and 1999 draft guidelines "are an expansion" of the 1986 final guidelines. What are the principle issues that remain to be resolved in order to finalize the guidelines, and when does the Agency anticipate finalizing these guidelines?

When the EPA's initial carcinogen risk assessment guidelines were published in 1986, they were the product of nearly two decades of risk assessment experience and scientific consensus-building. Their intended purpose was threefold: to capture current scientific thinking and approaches for conducting and evaluating risk assessments; to provide guidance to Agency risk assessors on the application of the principles and approaches described in the guidelines, thereby fostering consistency in the Agency's risk assessments; and to communicate to the public regarding the Agency's approaches to risk assessment.

Since publication of the 1986 guidelines, EPA has gained considerable experience in applying cancer risk assessment approaches. Likewise, the science of risk assessment and toxicological testing has continued to evolve. At the same time, the EPA has had to address situations not explicitly discussed in the 1986 guidelines, e.g., judging the human relevance of mode of action data developed through animal studies and assessing the potential carcinogenic risk to children. Revision of the 1986 carcinogen risk assessment guidelines is intended to consolidate the Agency's experience since the original guidelines were published. It will also provide more comprehensive and transparent guidance on topics not fully developed in the earlier guidelines as recommended by the National Academy of Sciences and other bodies, as well as provide flexibility to accommodate anticipated advances in the science. As in any scientific endeavor, the Agency anticipates that approaches to cancer risk assessment will evolve. The Agency gains experience in applying these approaches and at some point consolidates that experience through issuing proposed and, eventually, final guidelines.

When the draft guidelines were proposed in 1996, most of the public comments favored the proposed revisions. This response can be attributed partly to the fact that the proposed guidelines represent the evolution of risk assessment methods rather than a "sea change" in those methods and were thought by a majority of the public to be in keeping with advancing knowledge on cancer assessment. In an associated Federal Register notice (Federal Register of June 25, 1996; 61 FR 32799) the Agency announced that, pending publication of the final revised guidelines, the principles and procedures of the proposed guidelines would be applied in part or in whole on a case by case basis for new assessments. Application of these approaches reflects the Agency's accumulated experience and provides the Agency with more experience to draw upon in finalizing the guidelines. This approach parallels the approach taken during the interim period between 1984, when the first set of guidelines were proposed, and 1986 when they were finalized.

EPA has announced that there are three actions that it would take before finalizing the guidelines. The first is to expand the 1996 draft to provide more guidance on assessing potential carcinogenic risk to children. Some commenters argued that mode of action studies conducted in adult animals may not support a conclusion that the substance would work the same way in developing organisms, and that if one cannot show there are no age-related differences, the Agency should not abandon the linear default. EPA is awaiting the Science Advisory Board's (SAB) final report on a July 1999 meeting that focused on the changes to the draft cancer guidelines that address children. However, based on the lack of consensus among the SAB committee members, EPA expects additional work will be required. The second and third actions are to test the approaches described in the guidelines for judging mode of action data in the case of chloroform and atrazine. The SAB review of the chloroform draft risk assessment occurred in October 1999 and the FIFRA Scientific Advisory Panel (SAP) review of atrazine this past June. Based on the chloroform review, the SAB expressed overall support for the Agency's approach for assessing mode of action data and offered some suggestions for improvements or clarification (April 2000). The Agency agrees with those recommendations and is addressing them. Likewise, the Agency will address any guidelines related recommendations that arise from the SAP atrazine review.

b. Does the Agency intend to use the draft cancer guidelines for its risk assessment of atrazine? In its July 6, 2000 response to the Committee, the Agency justifies its reliance on the 1999 draft guidelines by stating, "the outcome of the Agency's preliminary hazard assessment would have been essentially the same if only the 1986 guidelines were available." Based on this statement, is it the Agency's position that because, in its view, "the outcome would have been the same," the Agency is justified in bypassing the procedural step of finalizing the guidelines prior to their use, thereby short-circuiting due process protections for those affected by the changes proposed in the draft guidelines?

The EPA statement quoted above appeared in a written response provided to the Committee on July 6 and in a *draft* desk statement that was prepared for EPA officials but never approved or used. The first sentence accurately represents EPA's impression of the SAP's oral opinions. The second sentence of this statement is accurate – the SAP did have a further recommendation regarding the proposed classification of atrazine as a likely human carcinogen – they recommended that EPA not classify it as such. Those not aware of the specific discussion at the SAP meeting could misinterpret this sentence. In subsequent correspondence we have been more explicit.

*b. On June 29, 2000, the day after the conclusion of the SAP meeting, **USA Today** featured a news story titled "Report: Common herbicide likely to cause cancer." This story appears to ignore the formal poll which found that the SAP members unanimously rejected the "likely human carcinogen" finding. Irrespective of the accuracy of the story, it is unfortunate that media reports about preliminary or pending Agency actions often results in public confusion about the safety of products undergoing Agency review. What steps does the Agency intend to take to rectify public misinterpretation potentially caused by this story? How does EPA intend to minimize further public misconception about its review of atrazine during the pendency of its review process?*

The ***USA Today*** story was published before the formal poll of the SAP members was taken. Therefore, it could not have accurately reflected this information.

EPA believes that the public's interest is best served when the Agency shares as much information as it can with the public, as early as possible, so that all concerned parties can evaluate the significance of the information. EPA has undertaken many efforts to inform the public of the procedures it uses to evaluate risks posed by pesticides and other hazardous chemicals and intends to continue such efforts. Furthermore, many institutions in the private sector also undertake efforts to educate the public about risk and risk assessment. With respect to atrazine, EPA will continue to follow the interim public participation process for non-organophosphorous pesticides, developed by the Agency and its stakeholders to promote transparency in the risk assessment and risk management processes, and the Agency's procedures for Special Review in Part 154 of Title 40 of the Code of Federal Regulations (CFR).

c. Please provide a transcript of the SAP proceedings on June 27-28, 2000. If a transcript was not created, please provide a detailed description of the findings of the SAP at its June 27-28, 2000 meeting.

While no transcript will be prepared for the June SAP meeting, the entire proceedings were tape recorded. A copy of this tape recording will be sent to your staff as soon as it is available.

The Agency is using the draft cancer guidelines in the risk assessment of atrazine. As explained above, shortly after EPA published the draft guidelines in 1996, it announced that it would apply the principles and procedures of the proposed guidelines in part or in whole on a case by case basis for new assessments, pending publication of the final revised guidelines. Furthermore, the SAB has identified atrazine as a case where use of the draft cancer guidelines would be especially useful.

Use of the draft cancer assessment guidelines does not short-circuit due process protections to which registrants are entitled. Cancer assessment guidelines, as well as other science policy guidelines, are intended to provide guidance to EPA personnel and decision-makers and to the public. As stated in the preface of each guideline document, neither draft guidelines nor final guidelines are binding on either EPA or any outside parties. Accordingly, EPA believes that its use of draft cancer assessment guidelines that have been released for public comment to guide its evaluation of science information in no way compromises the rights of any segment of the public.

c. *Will EPA honor its commitment to finalize the guidelines prior to revising the cancer risk assessment for atrazine?*

The statement in Marcia Mulkey's January 1999 letter was a reflection of the Agency's expectation at that time that the issues to be resolved in the draft guidelines could be handled quickly. Use of the draft guidelines in evaluating atrazine and chloroform will help achieve resolution of outstanding issues effectively. Furthermore, the atrazine SAP meeting discussions suggest that the cancer guideline's use in the atrazine risk assessment may not be of critical importance since the panel may recommend that the Agency not regulate atrazine on the basis of carcinogenicity. The Agency's basic commitment is to sound science and it will always pursue that commitment to the best of our abilities.

2. *At a meeting with Committee staff on July 6, 2000, EPA officials indicated that a poll taken during the June 27-28, 2000 meeting of the Scientific Advisory Panel (SAP) to review EPA's preliminary hazard characterization document concluded that SAP members unanimously rejected consideration of atrazine as a "likely human carcinogen." However, in an EPA desk statement issued after the SAP meeting and in a written response provided to the Committee on July 6, 2000, EPA states: "The SAP's preliminary position on EPA's draft hazard assessment signals agreement with the Agency's proposed mode of action for cancer and with the agency's assessment of potential for developmental and reproductive health effects . . . . The panel provided further recommendations regarding the Agency's proposed classification of atrazine as a likely human carcinogen."*

a. *Please reconcile the Agency's desk statement and subsequent written communication to the Committee with the outcome of the poll taken at the SAP meeting that unanimously concluded that atrazine should not be classified as a "likely human carcinogen." Does the Agency now believe the desk statement is misleading regarding the SAP meetings, and if not, why not?*

d. Please describe the process the SAP will employ to complete its consideration and issuance of a report on the preliminary hazard characterization for atrazine. When does the Agency anticipate that the SAP report will be issued?

The SAP's procedures for conducting peer reviews are specified in its Federal Advisory Committee Act (FACA) charter. During the public meeting, the SAP chair makes assignments for preparing the written report. All reports from the panel and subpanels are reviewed and approved by the chartered panel and approved by the SAP Chair before the report is transmitted to the Agency. The SAP will follow this procedure for the atrazine review as well. EPA anticipates receiving the SAP report on the preliminary hazard characterization for atrazine by the end of September.

3 *Because triazines, including atrazine, are under "special review" by EPA, FIFRA reregistration and FQPA tolerance reassessment, the established review processes and opportunities for public participation may be confusing for interested parties to follow.*

a. Please describe all anticipated opportunities for public review, public participation and public comment on the ongoing atrazine risk assessment that will be available prior to the Agency conclusion of the special review.

As you noted, EPA is conducting a reregistration and tolerance reassessment review of atrazine simultaneously with the triazine Special Review. In conducting these reviews, EPA will generally follow the interim procedures for public participation in reregistration and tolerance reassessment that were developed by the Agency and its stakeholders to promote transparency in the risk assessment and risk management processes and the procedures for Special Review in 40 CFR Part 154. EPA's stakeholders have clearly communicated to the Agency their wishes to comment on draft risk assessments and risk management plans. The Agency published its interim procedures for public participation for non-organophosphorous pesticides in the Federal Register of March 15, 2000 (65 FR 14200) and has extended the comment period on this notice. Additionally, EPA is working with the Committee to Advise on Reassessment and Transition, a subcommittee of the National Advisory Council for Environmental Policy and Technology recently formed under FACA, to refine the proposed public participation process.

In addition to the opportunities for stakeholder participation provided for in the interim procedures for public participation for non-organophosphorous pesticides, EPA regularly meets with stakeholders to discuss the atrazine review. EPA will continue to encourage meetings with the public on matters concerning the atrazine review. The specific opportunities for public involvement in the atrazine review are outlined in our response to question 3.b., below.

b. For FQPA review of non-organophosphates, EPA has established an interim public participation process that includes review of the risk assessment by the U.S.

Department of Agriculture, the product registrant, as well as a public comment period on the risk assessment. How do the steps in the FQPA interim public participation process relate to the next steps in the special review of atrazine?

The next steps in the reregistration and tolerance reassessment of atrazine and in the Special Review of the triazine herbicides (atrazine and simazine) include:

- SAP's submission of its written report which will be released to the public through the OPP docket and the Agency's website;
- EPA's evaluation of this report;
- Revision of the Agency's hazard assessment and characterization of atrazine's carcinogenic and non-carcinogenic effects (i.e., endocrine disruption potential).
- Release for public comment, under the interim public participation process, the revised hazard assessment for atrazine and the preliminary comprehensive health effects risk assessment covering acute, chronic, and cancer dietary, occupational, and aggregate (i.e., food plus water) exposures. The Agency will also release for public comment the preliminary environmental risk assessment.
- The preliminary health effects risk assessment for atrazine will then be used in the reregistration, tolerance reassessment, and Special Review determinations.
- Any Special Review document would be subject to a separate public comment period on both the proposed and final decision.
- EPA currently expects to wait for critical toxicity data on simazine, expected in mid-2001, before performing the risk assessment of simazine.
- EPA is considering whether it must complete the Special Review of the triazines or assess cumulative risk of exposures to atrazine and any other pesticide that has a common mechanism of toxicity before completing the tolerance reassessment and reregistration review of atrazine. EPA has not decided whether it would publish an interim or provisional RED on atrazine before completing the triazine Special Review or conducting a cumulative risk assessment.

c. Does EPA intend to issue a revised hazard characterization for atrazine prior to Issuance of a Position Document 2-3? Identify all opportunities for public participation available prior to issuance of Position Document 2-3. When does EPA anticipate making Position Document 2-3 on atrazine available for comment?

The Agency is planning to release the preliminary comprehensive risk assessment as soon as it is completed. At the time the preliminary risk assessment is released, all supporting documents, including the revised hazard assessment, will be released for public review and comment. As explained above, there are many uncertainties in the triazine risk assessment process that could affect the outcome and timing of the Special Review. Accordingly, the Agency cannot at this time predict when it will issue a Position Document 2-3 or any other Position Document on the triazine Special Review.

Regarding the atrazine risk assessment schedule, a crucial step in developing the risk assessment is receiving the final SAP report. Assuming the SAP report is forwarded to EPA within the next few weeks, EPA expects to complete the preliminary human health and ecological risk assessments for atrazine in Fall 2000.

d. Please describe the remaining steps necessary to complete adequate peer review of the Agency's risk assessment of atrazine and the studies underlying that risk assessment.

At the July 6 meeting with staff of the House Committee on Commerce, agency officials described the peer review process for published studies conducted by EPA researchers that entails internal peer review and review by experts selected by the publication's editors. As explained at that meeting, there is no corresponding peer review process for unpublished studies sponsored by the pesticide registrant. As part of its review of EPA's weight-of-evidence assessment, the SAP would examine the design and conduct of studies that EPA relied upon in its risk assessment. It should also be noted that under the requirements of chemical Special Review, EPA is required to have SAP peer review.

With respect to peer review of the Agency's risk assessment of atrazine, EPA has not determined whether there are any other issues regarding the risk assessment of atrazine or the triazine herbicides for which further peer review by an expert committee such as the SAP or SAB would be needed. As explained above, it is not possible to predict the path that these reviews are likely to take.

4. A significant issue under consideration as part of EPA's risk assessment of atrazine relates to several studies that purport to identify non-cancer effects associated with atrazine. While concerns have been raised about the availability of these newer studies, in its written response to the Committee on July 6, 2000, EPA indicated that these "lines of investigation" have been underway for several years, dating back as far as Summer 1994 regarding the reproductive toxicity of atrazine.

a. If these "lines of investigation" have been underway for as many as six years, please explain in detail why the Agency concluded in its December 1999 draft hazard characterization for atrazine that "[w]hile the animal data remain unclear regarding the potential for a susceptible period of increased cancer risk due to prenatal exposures throughout a lifetime, there is no indication that fetuses or young children (i.e., prepubertal stage) are susceptible to this mode of carcinogenic action."

This statement reflects EPA's understanding of the data available in late 1999 and focuses only on the cancer hazard posed by atrazine. Although the registrant, EPA's Office of Research and Development and academic researchers have been investigating the atrazine mode of action for several years, some of the studies needed for the more comprehensive hazard assessment were not published until early 2000. It is this additional information that allowed EPA to consider a single mode of action that may

lead to both cancer and non-cancer effects. Because key studies were unavailable at the time, the analysis in the December 1999 draft hazard characterization was incomplete.

b. Furthermore, please describe in detail why the Agency appears to have abruptly changed its course six months later in its June 2000 draft hazard characterization, in which the Agency states: "The consequence in children due to the neuroendocrine mode of action would depend upon the developmental stage of exposure and the duration of exposure. For example, prepubertal exposures would most likely result in developmental effects, and postpubertal exposure may result in a variety of health consequences, including cancer."

As described in material provided to the Committee at the July 6 meeting, EPA completed several new studies in late 1999 and early 2000 on the endocrine-disrupting effects of exposures that occur before puberty, including prenatal exposure. EPA has discussed findings of all of these studies with the registrant and presented some of the work in scientific conferences. In three cases, EPA provided the manuscripts of as yet unpublished studies to the registrant.

In June 2000, EPA updated the draft hazard characterization to add the finding that the atrazine mode of action that produces cancer when exposure occurs after puberty produces developmental effects, but not cancer, when exposure occurs before puberty, including prenatally. The June 2000 draft document reiterated that it is not possible to assess whether prenatal exposures result in cancer later in life via a mode of action not observed in post-pubertal or adult animals.

At the June meeting, the SAP expressed its support for EPA's interpretation of the data on the endocrine disrupting effects of atrazine, including the developmental effects resulting from prepubertal exposures.

5. Please provide a table describing the remaining steps and anticipated time-line for completing the Agency's special review of atrazine.

The next steps in the Special Review of the triazines are outlined above in response to question 3.b. As explained above, the Agency's Special Review considers the hazards posed by the triazine herbicides and includes simazine as well as atrazine.

Regarding the atrazine risk assessment schedule, a crucial step in developing the risk assessment is receiving the final SAP report. Assuming the SAP report is forwarded to EPA within the next few weeks, EPA expects to complete the preliminary human health and ecological risk assessments for atrazine in Fall 2000.